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International Application No.: **PCT/US03/10840**

International Filing Date : **09 April 2003**

Title : **Oligomeric Compounds Having Modified
Phosphate Groups**

Applicant : **Isis Pharmaceuticals, Inc.**

**LETTER ACCOMPANYING AMENDMENT AND
STATEMENT UNDER PCT ARTICLE 19**

International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20
Switzerland

Dear Sir, Madam:

In response to the International Search Report mailed 10 September 2004, for the above-identified International Patent Application, enclosed is an Amendment Under Article 19. Sheets numbered 96 and 99 are enclosed to replace originally submitted sheets 96 and 99 of the claims.

Claims 1 and 24 are amended in the replacement sheets. The basis for the amendments can be found, for example, at page 10, lines 5-7 of the paragraph immediately above paragraph 26.

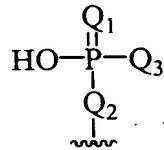
An edited version of the originally submitted claims is attached and shows the changes that have been made to the claims.

Respectfully submitted,

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- oligonucleotide, an oligonucleoside or said modified phosphate group; each X_1 and X_2 is, independently, O or S wherein at least one X_1 is S; n is from 3 to 48; and wherein at least one of J_1 , J_2 , J_3 , T_1 or T_2 is said modified phosphate group.
2. The oligomeric compound of claim 1 wherein Q_1 is S.
 3. The oligomeric compound of claim 1 wherein Q_2 is S.
 4. The oligomeric compound of claim 1 wherein Q_3 is CH_3 .
 5. The oligomeric compound of claim 1 wherein J_1 is said modified phosphate group.
 6. The oligomeric compound of claim 1 wherein at least one J_2 is said modified phosphate group.
 7. The oligomeric compound of claim 1 wherein J_3 is said modified phosphate group.
 8. The oligomeric compound of claim 1 wherein R_1 is a modified phosphate group.
 9. The oligomeric compound of claim 1 wherein at least one R_2 is a modified phosphate group.
 10. The oligomeric compound of claim 1 wherein R_3 is a modified phosphate group.
 11. The oligomeric compound of claim 1 wherein R_1 , R_3 and each R_2 is



wherein

one of Q_1 and Q_2 is S and the other of Q_1 and Q_2 is O;

Q_3 is OH or CH_3 ;

R_1 , R_3 and each R_2 is, independently, hydrogen, hydroxyl, a sugar substituent group, or a protected sugar substituent group or a phosphorthioate monoester;

each X_1 and X_2 is, independently, O or S wherein at least one X_1 is S; and

n is from 3 to 48;

wherein at least one of X_1 , X_2 , J_1 , J_2 , and J_3 is said modified phosphate group.

25. The oligomeric compound of claim 24 wherein Q_1 is S.

26. The oligomeric compound of claim 24 wherein Q_2 is S.

27. The oligomeric compound of claim 24 wherein Q_3 is CH_3 .

28. The oligomeric compound of claim 24 wherein J_1 is said modified phosphate group.

29. The oligomeric compound of claim 24 wherein at least one J_2 is said modified phosphate group.

30. The oligomeric compound of claim 24 wherein J_3 is said modified phosphate group.

31. The oligomeric compound of claim 24 wherein R_1 is a modified phosphate group.

32. The oligomeric compound of claim 24 wherein at least one R_2 is a